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## Resting-State Co-Activation Patterns in Pre-Dementia Alzheimer's Disease Patients: A Potential Early Marker?

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Alzheimer's disease (AD) is the most common neurodegenerative disorder, leading to cognitive decline, dementia, and death. It is marked by amyloid beta accumulation and neurofibrillary tangles of hyperphosphorylated tau, disrupting synaptic function and contributing to cognitive impairment. AD progresses through stages, from preclinical AD (biomarker evidence without symptoms) to prodromal AD (mild cognitive impairment with preserved daily function).

Resting-state fMRI (rs-fMRI) assesses whole-brain functional connectivity (FC) by measuring synchronized activity across regions. Traditional static FC analyses reveal reduced network efficiency, particularly in the default mode network (DMN), while dynamic FC captures temporal fluctuations, offering a more sensitive measure. Large-scale co-activation patterns (CAPs) provide deeper insights into resting-state brain dynamics.

The EPAD database, a multi-center cohort of 1,500 non-demented individuals, includes neuroimaging, CSF biomarkers, and neuropsychological data. A recent study using eigenvector centrality highlighted alterations in early AD. CAP analysis, as a complementary approach, offers novel insights into AD-related network dysfunction by comparing CAP metrics in healthy controls and pre-dementia AD. This study aims to advance understanding of CAPs in AD and assess their potential as early biomarkers for disease detection and progression.